

REMARKS

Priority

In the Office Action dated October 9, 2009 ("Office Action"), the Examiner indicates that the priority for the presently claimed invention as a whole is September 30, 1996 (*see* Office Action, page 4). A Declaration by all inventors, in six counterparts, claiming priority to U.S. Application No. 08/720,487, filed September 30, 1996 is submitted herewith. Applicants respectfully request that this Declaration be entered into the record of the application.

Claims

Claims 125, 126, 128, 131-138, and 142-160 have been found to be free of the art of record (*see* Office Action dated July 28, 2009, page 6, paragraphs 11 and 12 and Office Action dated October 9, 2009). The only issues outstanding with respect to these claims are an obviousness-type double patenting rejection over a co-owned patent, US Patent No. 5,876,727 (the "'727 patent"),¹ and a rejection for indefiniteness under 35 USC § 112.

Claims 125, 126, 128, 131-138, and 142-160 have been canceled by this Amendment, and have been transferred to applicants' co-pending Application No. 11/472,215, which has been terminally disclaimed over the co-owned '727 patent, rendering the obviousness-type double patenting rejection of the transferred claims moot. The transferred claims have also been amended to address the outstanding objection and rejections under 35 USC § 112, second paragraph for indefiniteness raised in the final office action in this examination. Allowance of amended claims 125, 126, 128, 131-138, and 142-160 will be sought in co-pending Application No. 11/472,215.

In the present application, new claims 161-168 have been presented. New claims 161-168 are directed to a species within the genus of claims 125, 126, 128, 131-138, and 142-160, which had been found to be free of the prior art of record. Upon entry of the present amendments, claims 161-168 will be pending in the present application. No new matter has been added by these amendments.

¹ Provisional obviousness-type double patenting rejections over *pending applications* are indicated (Final Office Action, page 11, paragraph 19). Since each of the pending applications are later filed, Examiner Steele indicated in our April 30, 2009 interview, that upon a finding of allowable subject matter, the instant application will be allowed to issue.

AN EARLY ALLOWANCE OF CLAIMS 161-168 IS REQUESTED

New claims 161-168 specify a species within the genus encompassed by the transferred claims 125, 126, 128, 131-138, and 142-160, and are free of the prior art of record for the very same reasons that the transferred claims 125, 126, 128, 131-138, and 142-160 were found to be free of the prior art of record.

The only unresolved rejection of the transferred claims 125, 126, 128, 131-138, and 142-160 is the obviousness-type double patenting, over claims 1-18 of the '727 patent, alone or in combination with US Patent No. 5,601,831 to Green ("Green"). Applicants believe that the new claims 161-168 are free of obviousness-type double patenting.

Applicants respectfully submit that new claims 161-168 are not obvious over the claims of the '727 patent, alone or in combination, with Green. New claims 161-168 are directed to nicotine conjugated to pseudomonas exotoxin – in particular nicotine modified to contain the CJ 11.1 branch.

Neither the pseudomonas exotoxin carrier *nor* the CJ 11.1 linker is specified in the claims of the '727 patent. Thus, two of the three elements of claims 161-168 are missing from the claims of the prior art. This defect is not cured by the disclosure of the '727 patent or the secondary reference, Green. Therefore, Applicants respectfully submit that *prima facie* obviousness as to claims 161-168 should not be found.

Even assuming *arguendo* that a *prima facie* case of obviousness were alleged, it is rebutted by evidence of unexpected results achieved with compositions commensurate in scope with claims 161-168. (A *prima facie* case of obviousness is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties. *In re Chupp*, 816 F.2d 643, 646; 2 U.S.P.Q.2d 1437, 1439 (Fed Cir 1987)). In this regard, the Applicants invite the Examiner's attention to the evidence of record showing unexpected advantageous and/or superior properties associated with the currently claimed conjugates.

As previously indicated in this record, nicotine is a small non-immunogenic hapten that actually *suppresses* the immune response. Thus, one of skill in the art would not have expected nicotine-carrier conjugates to induce a nicotine-specific immune response (*see* specification, page 19, lines 13-19; page 57, lines 31-35; and page 103, lines 32-34; *see also* Geng *et al.*, "Effects of Nicotine on the Immune Response I: Chronic Exposure to Nicotine Impairs Antigen Receptor-Mediated Signal Transduction in Lymphocytes," *Toxicol. Appl. Pharmacol.* 135:268-278 (1995) (reference C93 of the Supplemental IDS filed January 26, 2009), Abstract and Discussion section at page 75, 3rd paragraph)).

The evidence in this record shows that the claimed compositions *unexpectedly* induce a nicotine-specific immune response in human subjects. *See*, Hatsukami *et al.*, “Safety and Immunogenicity of a Nicotine Conjugate Vaccine in Current Smokers,” Clin. Pharmacol. Ther. 76:456-67 (2005) (“Hatsukami,” reference C82 of the Supplemental IDS filed June 12, 2008). Hatsukami describes the surprising properties of an aminomethylnicotine conjugated to pseudomonas exotoxin (NicVAX), *i.e.*, nicotine conjugated to CJ 11.1 as specified in claims 161-168. The Phase II clinical trials for NicVAX show that the aminomethylnicotine-pseudomonas exotoxin conjugate vaccine induces a nicotine-specific antibody response in human subjects (*see* Hatsukami) and that there is a clear dose response relationship between dose of conjugate vaccine and mean concentration of nicotine-specific antibodies in serum (*see*, Hatsukami, page 464, right col., first full paragraph, and Figures 1 and 3). This study demonstrated that 6 out of 16 patients who received the vaccine were able to abstain from smoking cigarettes for at least 30 days during the study, as compared to 2 out of 23 patients that received placebo.

This clinical trial demonstrates the surprising result that aminomethylnicotine conjugated to a pseudomonas exotoxin can be used efficaciously as a vaccine to elicit an antibody response to nicotine to treat nicotine addiction. Thus, these clinical trial results support the unexpected advantageous properties associated with the conjugates of claims 161-168.

For the foregoing reasons, Applicants respectfully assert that claims 161-168 are patentable over claims 1-18 of the '727 patent, alone or in combination, with Green.

CONCLUSION

Applicants respectfully request that the Examiner consider the amendments and the remarks made herein, and that the Examiner enter them into the record for the present application. An early allowance of claims 161-168 is earnestly sought. The Examiner is invited to contact the undersigned attorney if a telephone call could help resolve any remaining items.

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